identifying at least one sequence region which is conserved among said plurality of nucleic acids and said RNA of a selected organism;

determining whether said conserved region has secondary structure; and

for said conserved region having secondary structure, identifying said secondary structure.

REMARKS

Claims 26-29 and 35-50 are pending in the present application. Claims 26 has been cancelled. Claim 42 has been cancelled and replaced with new claim 51. Claims 35 and 39-41 have been amended. Upon entry of the present amendment, claims 27-29, 35-41 and 43-51 will be pending.

As a preliminary matter, Applicants thank the Examiner for indicating that claim 42 is allowable if rewritten to incorporate the language of the recited base claim. Applicants have rewritten claim 42 as new claim 51. No change in claim scope has been made.

I. The Claimed Invention Is Novel

A. The Williams Reference

Claims 26 and 35 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Williams *et al.*, *Nuc. Acids. Res.*, **1994**, *22*, 4660-4666 (hereinafter, the "Williams reference"). Claim 26 has been cancelled. Applicants traverse the rejection as it is applied to claim 35 and respectfully request reconsideration because the Williams reference does not teach every feature recited in claim 35.

The standard for anticipation under § 102(b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). The Office Action mistakenly asserts at page 5 that the Williams reference teaches all the limitations of claim 35. Nowhere, however, does the Office Action identify where the Williams reference teaches the method of identifying the molecular interaction site recited in claim 35. Indeed, the Williams reference is completely silent in regard to any methodology used to identify a "molecular interaction

site." Thus, the Williams reference does not anticipate claim 35. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

B. The Garcia Reference

Claims 27-29 and 35 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over Garcia *et al.*, *J. Mol. Biol.*, **1995**, *254*, 247-259 (hereinafter, the "Garcia reference"). Applicants traverse the rejection and respectfully request reconsideration because the Garcia reference does not teach or suggest every feature recited in the claims.

The Garcia reference reports a solution structure of the ribosome binding domain of *E. coli* translation initiation factor IF3. The Garcia reference also reports that IF3 interacts with 16S RNA. Significantly, however, the Garcia reference fails to teach or suggest an oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site, as recited in independent claims 27 and 35. In addition, the Garcia reference is completely silent in regard to any methodology used to identify a "molecular interaction site," in regard to claim 35. Thus, the Garcia reference does not anticipate or render obvious claims 27-29 or 35. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) or, alternatively, 35 U.S.C. § 103(a) be withdrawn.

C. The Gutell Reference

Claims 35-41 and 43-50 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over Gutell *et al.*, *Nuc. Acids Res.*, **1993**, *21*, 3051-3054 (hereinafter, the "Gutell reference"). Applicants traverse the rejection and respectfully request reconsideration because the Gutell reference does not teach or suggest every feature recited in the claims.

The Gutell reference illustrates proposed secondary structure models for 16S and 16S-like rRNAs for *E. coli*, yeast, and *C. elegans*. As recognized in the Office Action, the Gutell reference does not identify a molecular interaction site or determine the secondary structure of a conserved region within the RNA. The Office Action mistakenly asserts, however, that these features are

simply inherent limitations. Prior to discussing inherency, Applicants point out that the Gutell reference fails to teach or suggest an oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site, as recited in claim 35. In addition, the Gutell reference fails to teach or suggest that the particular interaction site, which is allegedly inherent, is also present in the RNA of at least one additional organism. There is also no teaching or suggestion in the Gutell reference of methodology used to identify a "molecular interaction site," let alone the methodology recited in claim 35.

To anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995). Further, to serve as an anticipation when a reference is silent about the alleged inherent characteristic, such gap in the reference may be filled by extrinsic evidence. Such evidence, however, must make clear that the missing descriptive matter is necessarily (*i.e.*, always) present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. *In re Oelrich*, 40 U.S.P.Q. 323 (C.C.P.A. 1981); *Continental Can Co. USA Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991). Significantly, the Office Action has not established that the recited inherent characteristics are necessarily present in the Gutell reference. Although the 16S rRNA has binding sites for molecules, a molecular interaction site is not necessarily present in all oligonucleotides that can be derived from the complete nucleotide sequence. Further, simply because the predicted secondary structure of 16S rRNA may contain some conserved regions (which the Office Action fails to particularly identify), any conserved regions that may be present are not necessarily present in all oligonucleotides that can be derived from the complete nucleotide sequence. Indeed, even the Gutell reference itself teaches that the 16S and 16S-like rRNA structure models for *E. coli*, yeast, and *C. elegans* are "divergent" (see page 3051, second column, objective 4). Thus, the Office Action has failed to provide any extrinsic evidence making clear that the missing descriptive matter is necessarily (*i.e.*, always) present in the thing described in the Gutell reference, and that it would be so recognized by persons of ordinary skill in the art.

Thus, the Gutell reference does not anticipate or render obvious claims 35-41 or 43-50. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) or, alternatively, 35 U.S.C. § 103(a) be withdrawn.

II. The Claims Are Clear And Definite

Claims 35-50 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Office Action asserts that there is no antecedent basis for the phrase "said target nucleic acid" in claims 35 and 39-41. Although Applicants submit that the claims are clear and definite as originally drafted, solely to advance prosecution of the present application, Applicants have amended claims 35 and 39-41 to be even more clear and definite by reciting "RNA of a selected organism" in place of "target nucleic acid." No new matter has been added and no change in claim scope is intended. In view of the amendment to the claims, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

III. The Claimed Invention Is Sufficiently Described

Claims 26 and 35-50 stand rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action mistakenly asserts that the specification fails to adequately describe that the claimed oligonucleotides do not comprise the iron response element (IRE). Applicants traverse the rejection as it is applied to claims 35-50 and respectfully request reconsideration because Applicants were clearly in possession of the claimed subject matter at the time of their invention.

In rejecting a claim under the first paragraph of 35 U.S.C. § 112 for lack of adequate written description, it is incumbent upon the examiner to establish that the originally-filed disclosure would not have reasonably conveyed to one having ordinary skill in the art that an applicant had possession of the now claimed subject matter. *Wang Laboratories, Inc. v. Toshiba Corp.*, 26 U.S.P.Q.2d 1767

(Fed. Cir. 1993). Adequate description under the first paragraph ***does not*** require literal support for the claimed invention. *In re Herschler*, 200 U.S.P.Q. 711 (C.C.P.A. 1979); *In re Edwards*, 196 U.S.P.Q. 465 (C.C.P.A. 1978); and *In re Werthein*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an applicant had possession of the ***concept*** of what is claimed. *In re Anderson*, 176 U.S.P.Q. 331 (C.C.P.A. 1973). Applicants' specification conveys such possession. Applicants teach at, for example, page 29, lines 27-28 that the IRE, a known regulatory region, was identified using the techniques disclosed in the present application. Applicants further teach in Example 1 on page 32, lines 1-13 of the specification, that the identification of the IRE serves as an excellent example of how Applicants' methodology works. Thus, one having ordinary skill in the art would have reasonably known that an oligonucleotide comprising the IRE was part of the prior art. In addition, one having ordinary skill in the art would also have known that, given the description of IRE in the prior art, Applicants' claimed invention did not include the IRE. Thus, Applicants maintain that the originally-filed disclosure would have conveyed to one having ordinary skill in the art that Applicants had possession of the concept of what is now claimed.

The Office Action cites *In re Grasselli* which is purported to support the position taken in the Office Action. The facts in *Grasselli* appear, however, to be quite different than the facts in the present case. In *Grasselli*, the applicants' originally-filed specification appears to have disclosed a catalyst comprising particular elements and/or metals. A negative limitation (*i.e.*, "said catalyst being free of uranium and the combination of vanadium and phosphorous") was added to a claim to remove at least one prior art reference. The originally-filed application, however, appears to have not expressly recited either uranium or the combination of vanadium and phosphorous, let alone their inclusion or exclusion. Thus, the Board in *Grasselli* held that the addition of the negative limitation, under these circumstances, was not adequately supported by the originally-filed specification.

The Examiner's attention is drawn to *Ex parte Parks*, 30 U.S.P.Q.2d 1234 (Bd. App. Pat. Int. 1993), a copy of which is enclosed herewith for the Examiner's convenience. In *Parks*, the originally-filed specification was completely silent in regard to whether a particular step within a claimed method was performed in the presence of a catalyst. The applicants in *Park*, in order to

remove a prior art reference, added a negative limitation (*i.e.*, "such decomposition being conducted in the absence of a catalyst"). The Board in *Parks*, however, held that given the technical context in which the particular step was performed, one having ordinary skill in the art would have understood the concept of performing the particular step was in the absence of a catalyst.

As stated above, the present application expressly recites the IRE and clearly teaches that it is part of the prior art. Thus, sufficient basis in the specification exists for excluding that which has been identified as being a part of the prior art. Thus, Applicants' originally-filed disclosure would have conveyed to one having ordinary skill in the art that Applicants had possession of the concept of what is now claimed. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

VII. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is encouraged to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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Paul K. Legaard
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Date: **July 24, 2001**

Enclosure: *Ex parte Parks*

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 26 and 42 have been cancelled.

New claim 51 has been added.

Claims 35 and 39-41 have been amended as follows:

35. (Amended) An oligonucleotide comprising a molecular interaction site that is present in the RNA of a selected organism and in the RNA of at least one additional organism, wherein said molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said RNA in said selected organism, wherein said oligonucleotide does not comprise the iron response element, wherein said molecular interaction site is identified by a method comprising:

comparing the nucleotide sequence of said [target nucleic acid] RNA of a selected organism with the nucleotide sequences of a plurality of nucleic acids from different taxonomic species;

identifying at least one sequence region which is conserved among said plurality of nucleic acids and said target nucleic acid;

determining whether said conserved region has secondary structure; and

for said conserved region having secondary structure, identifying said secondary structure.

39. (Amended) The oligonucleotide of claim 35 wherein said [target nucleic acid] RNA of a selected organism is present in a eukaryotic cell.

40. (Amended) The oligonucleotide of claim 39 wherein said [target nucleic acid] RNA of a selected organism is selected from the group consisting of mRNA, pre-mRNA, tRNA, rRNA, and snRNA.

41. (Amended) The oligonucleotide of claim 35 wherein said [target nucleic acid] RNA of a selected organism is present in a prokaryotic cell.

51. (New Claim) An oligonucleotide comprising a molecular interaction site that is present in the RNA of a selected organism and in the RNA of at least one additional organism, wherein said molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said RNA in said selected organism, wherein said oligonucleotide does not comprise the iron response element, wherein said molecular interaction site is identified by a method comprising:

comparing the nucleotide sequence of said target nucleic acid with the nucleotide sequences of a plurality of nucleic acids from different taxonomic species, wherein said nucleotide sequence of said RNA of a selected organism is determined by assembling a plurality of expressed sequence tags;

identifying at least one sequence region which is conserved among said plurality of nucleic acids and said RNA of a selected organism;

determining whether said conserved region has secondary structure; and

for said conserved region having secondary structure, identifying said secondary structure.